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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/526,329	03/15/2000	Carlo M. Croce	CR001.Np003	9316

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EXAMINER	
BRUMBACK, BRENDA G	
ART UNIT	**PAPER NUMBER**
1642	6

DATE MAILED: 01/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/526,329	CROCE ET AL.	
	Examiner	Art Unit	
	Brenda G. Brumback	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-93* is/are pending in the application.

4a) Of the above claim(s) *6,7,17-21,25-28 and 30-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-16,22-24 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I in Paper No. 5 is acknowledged. Claims 1-93 are pending. Claims 6, 7, 17-21, 25-28, and 30-93 are withdrawn from consideration as directed to a nonelected invention. Claims 1-5, 8-16, 22-24, and 29 are under examination.

Specification/Drawings

2. The disclosure is objected to because of the following informality. The Brief Description of the Drawings in the Specification references drawings of 10 Figures; however, only drawings of Figures 1-4 were filed with the present specification. Correction is required. Applicant is cautioned against the introduction of new matter in addressing this objection.

Additionally, the Brief Description of the Drawings should be amended to reference each of the drawings filed by number. For example, Fig. 3 should be amended to Fig. 3A-3D, etc.

The specification is objected to for the presence of aberrant punctuation marks; at page 19, lines 7 and 16, the double and triple question marks appear to be typographical errors. Correction is required.

The disclosure is also objected to because of the following informality. The address of the American Type Culture Collection found on page 10 of the specification (first occurrence at line 2) is incorrect, as the ATCC has relocated. The present address is 10801 University Blvd.,

Manassas, VA 20110-2209. Amendment of the disclosure to indicate the current address is required.

Specification

3. Claims 14, 23, and 29 are objected to for informalities of grammar. In claim 14, last line. the "an" should be amended to -- a --. In claim 23, last two lines, the "and" should be deleted and the "an" amended to -- a --. In claim 29, third line, "it" should be amended to -- its--.

Claim Rejections - 35 USC § 112

4. Claims 1-5, 8-16, 22-24, and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims recite a Tcl-1b protein. While Tcl-1 is an art recognized name for a particular protein, the name Tcl-1b appears to be applicant's. Applicant's specification discloses *TCL-1b* as a third member of the *TCL1* gene family (see page 1, lines 17-20) located at 14q32.1 (see page 3, lines 5-6) and discloses a sequence for the *TCL-1b* gene (SEQ ID NO:40) (see page 14, line 32). However, it is not clear from applicant's disclosure whether the *TCL-1b* gene encompasses only the gene consisting of the sequence of SEQ ID NO:40 or whether other genes are encompassed. Furthermore, if additional gene products are encompassed within the definition of a Tcl-1b protein, the disclosure does not appear to teach the metes and bounds of

these genes. Therefore, the metes and bounds of the claimed invention cannot be determined and the claims are indefinite.

Claims 2, 5, 8, and 11 recite "a" or "an" amino acid sequence of SEQ ID NO:39 or 38. It is not clear if the claims are intended to encompass the entire referenced sequence of whether the claims also encompass some undefined portion thereof. Absent a specific teaching of what is encompassed, the metes and bounds of the claimed invention cannot be determined and the claims are indefinite.

Similarly, claims 3 and 4 recite "an 18 nucleotide portion"; claim 12 recites "a 50 nucleotide portion"; and claims 14 and 23 recite "an 25 nucleotide portion". It is not clear whether the recited portions must be contiguous or whether noncontiguous portions are also encompassed.

Claims 13, 14, and 23 are drawn to an isolated nucleic acid capable of hybridizing under "stringent" conditions ..." The disclosure fails to teach the metes and bounds of "stringent" conditions. Therefore, the metes and bounds of the claimed invention cannot be determined and the claims are indefinite.

Claims 15, 16, and 29 recite a nucleotide sequence complementary to "at least a part" or "hybridizable". The phrase "at least a part" renders the claim indefinite because the metes and bounds of the recited "part" are unclear. Additionally, the term "hybridizable" renders the claims indefinite unless the specific conditions under which hybridization occurs are delineated.

5. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description" rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the "written description" inquiry, is *whatever is now claimed*" (see page 1117).

A review of the language of the claim indicates that these claims are drawn to a genus, i.e., the genus of Tcl-1b proteins encompassing the full length protein and fragments thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the

genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention".

There is a single species of the claimed genus disclosed that is within the scope of the claimed genus, *i.e.* the Tcl-1b protein consisting of amino acids 1-128 of SEQ ID NO:39. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses numerous species that are not further described. There is substantial variability among the species.

One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of which comprises a myriad of possible fragments of the Tcl-1b protein, as well as the full length protein. The skilled artisan cannot envision the detailed chemical structure of the encompassed fragments. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

6. Claims 1-5, 8-16, and 22-24, and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of

the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to an isolated nucleic acid comprising a nucleotide sequence encoding a Tcl-1b protein. The specification teaches that the Tcl-1b protein is useful for diagnosis and therapy of disease states associated with chromosonal abnormalities, as in certain T-cell malignancies (see pages 1-3).

The state of the prior art and the predictability or lack thereof in the art: As for diagnostic application of the claimed protein, Pekarsky et al. (Proc. Natl. Acad. Sci. 96:2949-2951, March 16, 1999) teach that the *TCL1b* gene is expressed, along with the *TCL1* gene in tissues other than malignancies, *i.e.*, spleen, tonsil, fetal liver, fetal kidney, fetal thymus, placenta, kidney, and fetal spleen (see page 2950, the paragraph bridging columns 1 and 2). Pekarsky et al. further teach that "Neither the *in vivo* function of Tcl1 nor the mechanism(s) of its oncogenic potential is known" (page 2951, column 1, fourth full paragraph).

Regarding therapy of disease states associated with chromosomal abnormalities, the art teaches that the efficacy of therapeutics is dependent upon factors such as solubility of the drug, bioavailability at the target site, attainment of effective plasma concentrations, solubility in tissues, biotransformation, toxicity, proteolytic degradation, immunological inactivation, rate of excretion or clearance (half-life), deactivation by the liver, hydrolysis in serum, binding to plasma protein, and in the case of antivirals, propensity for emergence of resistant strains (see Benet et al., pp. 3-32, in The Pharmacological Basis of Therapeutics, 8th ed., 1990, page 3, first

paragraph; page 5, second column, last partial paragraph, first two sentences; page 10, the paragraph bridging columns 1 and 2; page 18, the paragraph bridging columns 1 and 2; page 20, last full paragraph; and the paragraph bridging pages 20 and 21 and footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO BD> APP>& Inter. 1992).

The amount of direction or guidance present and the presence or absence of working examples: The specification contains only a general disclosure that the nucleic acid encoding the Tcl-1b protein has diagnostic and therapeutic applications (see page 5, lines 30-32). There are no specific teachings or disclosure as to how to utilize the claimed nucleic acids so as to effect diagnosis of any specific disease. There are no working examples demonstrating development or application of the nucleic acid or the protein as diagnostics.

Regarding therapy of disease states associated with chromosomal abnormalities, as in T-cell malignancies, there are no teachings in the disclosure as to how to administer any of an antisense molecule, the protein product, an antagonist of the protein, or an antibody directed against the protein, in order to achieve therapeutic benefit against a particular disease. There are no working examples teaching administration of any of the claimed nucleic acids as therapeutics.

The breadth of the claims and the quantity of experimentation needed: Because the claims are drawn to nucleic acid molecules for which applicant's disclosure lacks guidance as to how to use for diagnosis or therapy of disease related to a chromosomal disorder and given the teachings of unpredictabliliy found in the art, it would require undue experimentation by one of skill in the art to be able to use the claimed invention.

Conclusion

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Sequence Search, Database EST, Accession No. AA825207, 1997 (Result 3, page 3) discloses a sequence with 99.4% local similarity from nucleotides 650 through 1152 of claimed SEQ ID NO:38.

Sequence Search, Database EST, Accession No. AI224367, 1997 (Result 6, pages 4-5) discloses a sequence with 100% local similarity from nucleotides 725 through 1131 of claimed SEQ ID NO:38.

Sequence Search, Database GenEmbl, Accession No. AB018563, 10/12/1998 (Result 5, pages 13-14) discloses a sequence with 99.8% local similarity from nucleotides 4968 through 6331 of claimed SEQ ID NO:40.

Sugimoto et al. (Cancer Research 59, 2313-2317, May 15, 1999) discloses the sequence depicted as Accession No. AB018563 in Database GenEmbl as a TCL1 like gene from the region next to the *Tcl1* locus (see the title).

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony

Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Official FAX telephone number is (703) 872-9306 and the After Final FAX telephone number is (703) 872-9307. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

BB
December 21, 2001

Brenda Brumback
Brenda Brumback,
Patent Examiner